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(57) Abstract

The present invention relates to dentifrices with improved flavour display comprising, flavour oil, a non–ionic block co–polymer, anionic or amphoteric surfactants, a fluoride ion source, water and wherein the dentifrice comprises a liquid carrier which forms a single, clear liquid layer.

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DENTIFRICE COMPOSITIONS

BACKGROUND OF THE INVENTION

A high standard of oral hygiene is essential for maintaining healthy gums and teeth. One step to achieving such oral hygiene is brushing regularly with a dentifrice formulated to provide some efficacy and protection against the bacteria and microbes which inhabit the oral cavity. In such respect it is recommended by dentists that consumers brush twice daily with a suitable product. There are many dentifrice compositions which contain active agents to prevent the beginnings of gum disease, calculus build-up and cavities. The active agents of a dentifrice are those agents which inhibit the formation of calculus and prevent the accumulation of plaque bacteria and other micro-organisms which are responsible for halitosis, plaque, caries and gum diseases such as periodontis and gingivitis. However it is not only important to the consumer that the dentifrice composition deliver the necessary active agents, it is also important that such compositions have excellent aesthetic properties such as flavour and foam.

Flavour is a highly desirable feature of a dentifrice. One of the first sensations the consumer notices upon mechanical agitation of the dentifrice, is the initial flavour impact delivered from the dentifrice, to the oral cavity during brushing. Immediately following brushing with a dentifrice, the mouth will usually feel refreshed.

Foam is a further highly desirable feature of a dentifrice. The foam produced by the mechanical agitation of the dentifrice in the mouth acts to disperse the dentifrice formulation in the oral cavity and deliver the active agents around the same. The extent to which a product foams provides an indication to the user that the dentifrice is achieving the desired cleaning benefits.

US 5,424,060 discloses the combination of two anionic surfactants, one of which being sodium alkyl sulfate with a non-ionic surfactant such as block co-polymers to provide an effective foaming action during brushing. Further, the non-ionic surfactant provides solubilising, dispersing and emulsifying activities relative to the other components of the dentifrice. There is no teaching in the document as to improved flavour display of a dentifrice containing these ingredients.

US 5,130,122 discloses a dental or oral hygiene product wherein the product can be an abrasive toothpaste comprised of a submicron emulsion of an absorptive oil such as mineral oils and vegetable oils in an aqueous medium. The product further contains ingredients such as abrasives, thickeners, sweeteners and flavours. Amongst the emulsifiers suitable for the invention, the patentee cites sodium lauryl sulfate, sodium lauryl sarcosinate and block co-polymers of propylene/ethylene oxide or mixtures thereof. There is no specific disclosure of the particular combination of block co-polymers and anionic surfactants.

US 4,069,310 claims a method for manufacturing a visually clear dentifrice comprising a water insoluble polishing agent, gelling agent, sodium lauroyl sarcosinate and a vehicle comprising water, sorbitol and glycerine. The document teaches that sodium lauroyl sarcosinate may be partially replaced by Pluronic F-68, however there is no teaching as to the extent of replacement.

WO 97/46214 discloses an antibacterial oral composition containing a mixed anionic/non-ionic surfactant system with a weight ratio from 14:1 to 9:1 respectively, with the optimal ratio being 9:1. A ratio of less than 9:1 is taught to produce a dentifrice with unsatisfactory taste characteristics. The mixed surfactant system is taught to increase the uptake and bioavailability of the antibacterial compound. Suitable surfactants disclosed include higher alkyl sulfates and polyoxyethylene-polyoxypropylene block co-polymers.

Nevertheless and despite the preceding discussion, there remains a need to deliver improved flavour impact from a dentifrice so as to provide for increased consumer acceptance of the product.

It has been discovered by the present inventors that a dentifrice with improved flavour delivery is achieved, when the dentifrice comprises, flavour oil, a non-ionic block co-polymer, anionic or amphoteric surfactants, a fluoride ion source, water and wherein the dentifrice comprises a liquid carrier which forms a single, clear liquid layer.

Therefore, it is an object of the present invention to provide improved flavour delivery from a dentifrice. It is also an object of the present invention to provide dentifrice compositions with improved flavour delivery through the use of flavour oil, anionic or amphoteric surfactants and non-ionic block co-polymer systems, a fluoride ion source and water, wherein the dentifrice comprises a liquid carrier which forms a single,

clear liquid layer. It is a further object of the invention to provide a dentifrice having improved flavour display and good foaming.

These and other objects of the present invention will become readily apparent from the detailed description which follows.

All percentages and ratios used herein are by weight of the total composition unless otherwise specified. All measurements are made at 25°C, unless otherwise specified.

SUMMARY OF THE INVENTION.

A dentifrice with improved flavour display comprising

(a) from 0.1% to 10% of a flavour oil;

(b) from 0.1% to 10% of a non-ionic block co-polymer;

(c) from 0.1% to 5.0% of a surfactant selected from amphoteric or anionic surfactants and combinations thereof;

(d) a fluoride ion source;

(e) from 10% to 90% of water;

wherein the dentifrice comprises a liquid carrier which forms a single, clear liquid layer.

DETAILED DESCRIPTION OF THE INVENTION

The term "dentifrice", as used herein, means liquid, paste or gel formulations unless otherwise specified. For the present invention, the term "liquid" dentifrice is as described in US 5,695,746. Preferably the dentifrice is a single homogeneous product, but it can also be a multiphase product such as a deep or surface striped dentifrice or multiphase product stored in a dual compartment. A deep or surface striped dentifrice is one where the dentifrice may comprise two or more separate layers which are in contact with each other. The separate layers may be a paste and a gel that when extruded from the tube, appear as combination paste/gel stripes. One of the layers must comprise all of the essential components, while the other layers may contain less than all of the essential components or may be any dentifrice formulation. Further, dentifrice compositions can be physically separated in a dentifrice dispenser. The dispenser may be a tube, pump, or any other container suitable for dispensing toothpaste. Dual compartment packages suitable for this purpose are described in U.S. Patent 4,528,180, issued July 9, 1985; U.S. Patent 4,687,663, issued August 18, 1987; and 4,849,213, issued July 18, 1989, all to Shaeffer. The compositions may intermix once dispensed. Alternatively, the dentifrice may be delivered from a kit containing two separate dispensers which are used to deliver two dentifrice compositions that are both used simultaneously. The dentifrice in its entirety,

being a single homogeneous product, or a multiphase product thereof, may be clear or opaque provided that it comprises a liquid carrier which forms a single, clear liquid layer.

The present compositions comprise essential components, as well as optional components. The essential and optional components of the compositions of the present invention are described in the following paragraphs.

The term "liquid carrier" as used herein means all components of the dentifrice formulation excluding; (a) inorganic solids with less than 0.1% solubility in water and (b) binders. By "binder" is meant a material added to increase the viscosity of the combined liquid components to above 0.1 Pascals, preferably above 1 Pascal and most preferably greater than 10 Pascals. The clear, single layer may be a solution or gel and is free from visually observable suspended solids.

The purpose of excluding components (a) and (b) from the liquid carrier, is to facilitate the visual observation of a single, clear liquid layer.

In most instances, if the liquid carrier is going to separate into two or more layers, it will do so within a short space of time after mixing, typically less than four hours, or even less than 1 hour. However, if necessary, and in order to decrease the time for determining whether there is a clear, single liquid layer present, the liquid carrier may be centrifuged for 10 minutes at 20 000 G. A suitable instrument for the centrifugation is a Beckman Avanti 30 centrifuge with type F0630 rotor.

For instance, when a liquid carrier of the present invention comprises tetrapotassium pyrophosphate and anionic surfactants comprising an alkyl sulfate moiety, potassium can complex to the alkyl sulfate chain and form potassium alkyl sulfate, an insoluble complex, which can remain suspended within, and cloud the liquid carrier. When a cloudy suspension of potassium alkyl sulfate is formed, this may occlude the visual observation of the number of layers of the liquid carrier. In order to overcome such an effect, observation may only be possible following centrifugation of the liquid carrier as described above.

Microemulsions, which are dispersions of very small droplet sizes, formed spontaneously without the input of work fall within the scope of the liquid carrier as herein described.

A dentifrice not falling within the scope of the invention would include a dentifrice whose liquid carrier formed two liquid layers upon preparation or standing.

In terms of clarity, the liquid carrier of the dentifrice preferably has a clarity index of less than about 100 nephetometric turbidity units (NTU), preferably less than about 50 NTU, even more preferably less than about 30 NTU, clarity being measured at 20°C using a Orbico-Hellige Series 965 Turbidity Meter calibrated over the range 0 to 99.9 NTU.

Flavour Oil

The dentifrice of the present invention comprises a flavour oil. The components of the flavour oil may be in the form of an oil, liquid, semi-solid, solid, or powder and may be of a natural and/or synthetic flavour origin. The term "flavour" according to the present invention means any essence, either natural or synthetic, or active agent (such as coolant agents), included in a composition to provide a palatable taste profile or physiological effect upon use. Various flavours can be used in the flavour oil of the present invention. The flavour oil generally consists of flavour components from the group consisting of peppermint, spearmint, cinnamon, spice, wintergreen, fruit, citrus, herbal, medicinal, and common food flavours (i.e. chocolate) and mixtures thereof. Illustrative, but nonlimiting examples of such components include peppermint oils such as Mentha piperita and Mentha arvensis; spearmint oils such as Mentha cardiaca and Mentha spicata; hydrocarbons such as limonene, caryophyllene, myrcene, and humulene; alcohols such as menthol, linalool, 3-decanol, and pinocarveol; ketones such as peperitone, menthone, spicatone, and l-carvone; aldehydes such as acetaldehyde, 3-hexanal, or n-octanal; oxides such as menthofuran, pepertione oxide, or carvyl acetate-7,7 oxide; acids such as acetic and ocenoic; and sulphides such as dimethyl sulphide. Components also include esters such as menthyl acetate, benzyl isobutyrate, and 3-octyl acetate. The esters are stable in compositions having a pH of about 7 or lower, and preferably a pH of about 4.5 or lower. The components may also consist of essential oils such sage oil, parsley oil, marjoram oil, cassia oil, clove bud oil, cinnamon oil, eucalyptus oil, anise oil, and mixtures thereof. The flavor components may also consist of flavour chemicals such as cinnamic aldehyde, eugenol, ionone, anethole, eucalyptol, methyl salicylate, oxanone, alpha-irisone, and mixtures thereof. Preferred are peppermint oils, spearmint oils, menthol, anethole, methyl salicylate, cinnamon oils, clove bud oils, oxanone, and mixtures thereof. Flavour components are described in more detail in Fenaroli's *Handbook of Flavor Ingredients*, Third Edition, Volumes 1 & 2, CRC Press, Inc. (1995), and Steffen Arctander's *Perfume and Flavour Chemicals*, Volumes 1 & 2, (1969). The flavour oil may additionally comprise components such as vanillin, ethyl vanillin, heliotropine, propenyl guaethol, vanilla extracts, veratraldehyde, 4-cis-heptenal, diacetyl, butyl lactate, ethyl lactate, methyl-para-tert-butyl phenyl acetate, gamma and delta hexalactone and heptalactone, benzodihydropyrone, butter starter distillate, delta tetradecalactone, butyraldehyde, and mixtures thereof. A physiological cooling agent may also be incorporated into the flavour oil. The coolant can be any of a wide variety of materials. Included among such materials are carboxamides, menthol, acetals, ketals, diols, and mixtures thereof. Preferred coolants

in the present compositions are the paramenthane carboxyamide agents such as N-ethyl-p-menthan-3-carboxamide, (known commercially as "WS-3") and mixtures thereof and menthone glycerine acetal (known commercially as "MGA"). Further disclosure of coolants suitable for the present invention are discussed in WO97/06695, incorporated by reference herein. The flavour oil is used in the present composition at levels of from about 0.1% to about 10.0%, preferably from about 0.5% to about 5.0%, and most preferably from about 0.1% to about 2.0%, by weight of the composition.

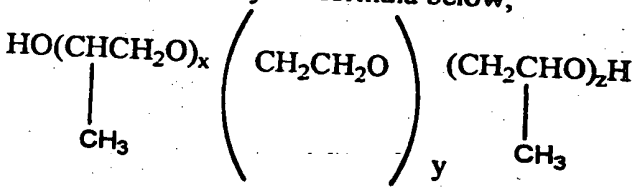
Non-Ionic Block Co-Polymer

The dentifrice of the present invention comprises a non-ionic block co-polymer.

The non-ionic block co-polymers of the present invention have a HLB ("hydrophilic-lipophilic balance") within the range of greater than 5 and more preferably greater than 10, to less than 40, preferably less than 30. Suitable non-ionic block co-polymers for the present invention are amine block co-polymers and polyoxyalkylene block co-polymers. Preferred are the polyoxyethylene-polyoxypropylene block co-polymers.

Amine block co-polymers are known commercially as poloxamines and are the polyoxyethylene, polyoxypropylene block polymers of ethylene diamine. Poloxamines are manufactured and sold with a wide range of structures and molecular weights with varying repeating units of ethylene oxide and propylene oxide and are commercially available from ICI under the Synperonic T tradename and from BASF under the Tetronic tradename.

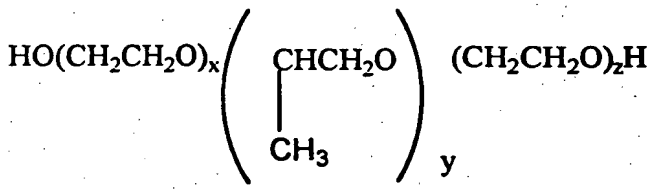
Polyoxyalkylene block co-polymers are typically polyoxyethylene-polyoxypropylene block co-polymers, also known commercially as poloxamers and meroxapols. These block co-polymers are manufactured and sold with a wide range of structures and molecular weights with varying repeating units of ethylene oxide and propylene oxide. Meroxapols are defined by the formula below;



wherein x, y and z are numerical values which define the average number of repeating units.

Liquid and low-melting meroxapols are commercially available from BASF under the Pluronic R® tradename.

The preferred non-ionic block co-polymers for the present invention are polyoxyethylene-polyoxypropylene block co-polymers, known commercially as poloxamers which are defined by the formula below;



wherein x, y and z are numerical values which define the average number of repeating units.

Polyoxyethylene-polyoxypropylene block co-polymers are stable and readily dispersible in aqueous systems. These surfactants are often further defined in terms of the molecular weight of the polyoxypropylene hydrophobic moiety and the percent weight of the polyoxyethylene hydrophilic moiety.

The polyoxyethylene-polyoxypropylene block co-polymers useful in this invention include the following poloxamers:

Poloxamer 101	Poloxamer 183	Poloxamer 234	Poloxamer 333
Poloxamer 105	Poloxamer 184	Poloxamer 235	Poloxamer 334
Poloxamer 108	Poloxamer 185	Poloxamer 237	Poloxamer 335
Poloxamer 122	Poloxamer 188	Poloxamer 238	Poloxamer 338
Poloxamer 123	Poloxamer 212	Poloxamer 282	Poloxamer 402
Poloxamer 124	Poloxamer 215	Poloxamer 284	Poloxamer 403
Poloxamer 182	Poloxamer 217	Poloxamer 288	Poloxamer 407

Liquid and low-melting poloxamers are commercially available from BASF under the Pluronic® tradename, ICI under the Synperonic tradename and Calgene under the Calgene Non-Ionic tradename. Preferred are those poloxamers containing from about 20% to about 90% ethylene oxide by weight, more preferred are those poloxamers containing from about 60% to 85% ethylene oxide by weight. Particularly preferred are Poloxamer 188, Poloxamer 235 and Poloxamer 407.

Non-ionic block co-polymers useful herein are those which are soluble in water. Particularly preferred herein are those non-ionic block co-polymers having a Ross Miles foam height (ASTM Method D-1173-53) measured in 0.1% aqueous solution at 26°C of greater than 5 mm and more preferably greater than 10 mm.

In general, the dentifrice of the present invention comprise from about 0.1% to 10.0%, preferably from about 0.1% to about 4.0%, more preferably from about 0.2% to about 3.0% of a non-ionic block co-polymer.

Preferably, the dentifrice of the present invention comprise from about 0.1% to 10.0%, preferably from about 0.1% to about 4.0%, more preferably from about 0.2% to about 3.0% of a polyoxyethylene-polyoxypropylene block co-polymer.

Anionic and Amphoteric Surfactants

The dentifrice of the present invention further comprises a surfactant selected from anionic and amphoteric surfactants.

Anionic surfactants useful herein include the water-soluble salts of alkyl sulfates or alkyl ether sulfates having from 8 to 20 carbon atoms in the alkyl radical (e.g., sodium alkyl sulfate), sulfoacetates, alkyl glyceryl sulfonates and the sarcosinates. Non-limiting examples of the anionic surfactants of this type which are suitable for the present invention are sodium decyl sulfate, sodium lauryl sulfosuccinate, sodium lauryl sulfate and sodium lauroyl sarcosinate. Preferably, dentifrices of the present invention comprise the anionic surfactant sodium lauryl sulfate.

The amphoteric surfactants useful in the present invention can be broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be a straight chain or branched and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic water-solubilising group e.g. carboxylate, sulfonate, sulfate, phosphate or phosphonate. Other suitable amphoteric surfactants are betaines, specifically cocomidopropyl betaine. Mixtures of amphoteric surfactants may also be employed.

In general, the dentifrice of the present invention comprise from about 0.1% to about 5.0%, preferably from about 0.5% to about 3.0%, and most preferably from about 1% to about 3.0% anionic or amphoteric surfactants, by weight of the composition.

Preferably, the dentifrice of the present invention comprises the mixture of anionic or amphoteric surfactant to non-ionic block co-polymer in a weight ratio from about 7:1, preferably about 2:1, most preferably about 1:1.

Fluoride Ion Source

A dentifrice of the present invention also comprises a fluoride source capable of providing free fluoride ions. Preferred soluble fluoride ion sources include sodium fluoride, stannous fluoride, indium fluoride, and sodium monofluorophosphate. Sodium fluoride is the most preferred fluoride ion source. Norris et al., U.S. Patent 2,946,725,

issued July 26, 1960, and Widder et al., U.S. Patent 3,678,154 issued July 18, 1972, disclose such fluoride ion sources as well as others.

The present compositions contain a fluoride source capable of providing from about 50 ppm to about 3500 ppm, and preferably from about 200 ppm to about 2500 ppm, more preferably from 500 ppm to 2000 ppm of free fluoride ions.

Total Water Content

Water is also contained in compositions of the present invention. Water used in the preparation of these compositions should preferably be of low ion content and free of organic impurities. The "total water content" of the dentifrice, as used herein, includes the free water which is added plus the water which is introduced with other materials, such as with sorbitol, silica, colour solutions, or surfactant solutions. The total water content of the dentifrice of the present invention is from about 10% to about 90%, preferably from about 20% to about 80%, more preferably from about 35% to about 65% by weight of the composition.

The percentage of water in the liquid carrier as aforementioned is generally from about 10% to about 95%, preferably from about 25% to about 95%, more preferably from about 40% to about 80%.

Additional Components

Humectants

Humectants are preferred components of the liquid carrier. The humectant serves to keep dentifrice compositions from hardening upon exposure to air and certain humectants can also impart desirable sweetness of flavour to dentifrice compositions. Suitable humectants for use in the invention include xylitol, glycerin, sorbitol (70% aqueous solution), polyethylene glycol, propylene glycol and combination thereof. If a mixture of humectants are used in dentifrice of the invention, wherein one of the humectants is sorbitol, the ratio of the second humectant to water should not exceed 1:2. The most preferred humectant is sorbitol. The total amount of humectant generally comprises from about 0.5% to 70%, preferably from about 5% to 60%, and more preferably from about 15% to about 55%, by weight of the compositions herein.

Xylitol may also provide a therapeutic effect, such as an antibacterial or anticaries effect. Suitable levels of xylitol in dentifrice of the present invention are from about 0.01% to about 25%, preferably from about 3% to about 15%, more preferably from

about 5% to about 12%, and most preferably from about 9% to about 11%, by weight of the composition.

Polyphosphate Source

Dentifrice of the present invention may include a polyphosphate source. For the purposes of the present invention a polyphosphate may also be a pyrophosphate salt. The preferred pyrophosphate salts include the dialkali metal pyrophosphate salts, tetra alkali metal pyrophosphate salts, and mixtures thereof. Disodium dihydrogen pyrophosphate ($Na_2H_2P_2O_7$), tetrasodium pyrophosphate ($Na_4P_2O_7$), and tetrapotassium pyrophosphate ($K_4P_2O_7$) are the preferred species. If present in dentifrice of the present invention, the pyrophosphate salt may be in one of three ways: predominately dissolved, predominately undissolved, or a mixture of dissolved and undissolved pyrophosphate.

Compositions comprising predominately dissolved pyrophosphate refer to compositions where at least one pyrophosphate ion source is in an amount sufficient to provide at least about 1.0% free pyrophosphate ions. The amount of free pyrophosphate ions may be from about 0.5% to about 10% and preferably from about 1.5% to about 5%, by weight of the composition. Free pyrophosphate ions may be present in a variety of protonated states depending on a the pH of the composition.

Compositions comprising predominately undissolved pyrophosphate refer to compositions containing no more than about 33% of the total pyrophosphate salt dissolved in the composition, preferably less than about 25% of the total pyrophosphate dissolved in the composition. Tetrasodium and disodium dihydrogen pyrophosphate salts are the preferred pyrophosphate salts in these compositions. Tetrasodium pyrophosphate or disodium pyrophosphate may be added as the anhydrous salt forms or the decahydrate forms. The insoluble pyrophosphate salt in the dentifrice is of a solid particle form, which may be its crystalline and/or amorphous state, with the particle size of the salt preferably being small enough to be aesthetically acceptable and readily soluble during use. The amount of pyrophosphate salt useful in making these compositions is any tartar control effective amount, and is generally from about 0.5% to about 10% and preferably from about 1.5% to about 5%, by weight of the composition. Some or all of the tetrasodium pyrophosphate may be undissolved in the product and present as tetrasodium pyrophosphate particles. Pyrophosphate ions in different protonated states (e.g., $HP_2O_7^{-3}$) may also exist depending upon the pH of the composition and if part of the tetrasodium pyrophosphate is dissolved.

Compositions may also comprise a mixture of dissolved and undissolved pyrophosphate salts. Any of the above mentioned pyrophosphate salts may be used.

The pyrophosphate salts are described in more detail in Kirk & Othmer, *Encyclopaedia of Chemical Technology*, Third Edition, Volume 17, Wiley-Interscience Publishers (1982), incorporated herein by reference in its entirety, including all references incorporated into Kirk & Othmer.

Optional agents to be used in place of or in combination with the pyrophosphate salt include such materials known to be effective in reducing calcium phosphate mineral deposition related to calculus formation. Agents included are synthetic anionic polymers [including polyacrylates and copolymers of maleic anhydride or acid and methyl vinyl ether (e.g., Gantrez), as described, for example, in U.S. Patent 4,627,977, to Gaffar et al., the disclosure of which is incorporated herein by reference in its entirety; as well as, e.g., polyamino propoane sulfonic acid (AMPS)], zinc citrate trihydrate, diphosphonates (e.g., EHDP; AHP), polypeptides (such as polyaspartic and polyglutamic acids), and mixtures thereof.

Polyphosphates useful in the present invention consist of two or more phosphate molecules arranged primarily in a linear or cyclical configuration, wherein the polyphosphates desired are those having around three or more phosphate molecules. The inorganic polyphosphate salts desired include tripolyphosphate, tetrapolyphosphate and hexametaphosphate, among others. Polyphosphates larger than tetrapolyphosphate usually occur as amorphous glassy materials. Preferred in this invention are the linear "glassy" polyphosphates having the formula:

$$XO(XPO_3)_nX$$

wherein X is sodium or potassium and n averages from about 6 to about 125. Preferred are polyphosphates manufactured by FMC Corporation which are commercially known as Sodaphos ($n \approx 6$), Hexaphos ($n \approx 13$), and Glass H ($n \approx 21$). These polyphosphates may be used alone or in an combination thereof.

The phosphate sources are described in more detail in Kirk & Othmer, *Encyclopaedia of Chemical Technology*, Fourth Edition, Volume 18, Wiley-Interscience Publishers (1996), incorporated herein by reference in its entirety, including all references incorporated into Kirk & Othmer. The polyphosphate source will typically comprise from about 0.5% to about 20%, preferably from about 4% to about 15%, more preferably from about 6% to about 10%, and most preferably from about 7% to about 9%, by weight of the dentifrice composition In compositions of the present invention.

Colouring and Sweetening Agents

Colouring agents may also be added to the dentifrice of the present invention. The colouring agent may be in the form of an aqueous solution, preferably 1% colouring

agent in a solution of water. Colour solutions generally comprise from about 0.01% to about 5%, by weight of the composition.

Sweetening agents can be added to the dentifrice. These include sodium saccharin, dextrose, sucrose, chlorinated sucrose, lactose, maltose, levulose, aspartame, sodium cyclamate, D-tryptophan, dihydrochalcones, xylitol, acesulfame, monoammonium glycyrrhizinate, and mixtures thereof. Sweetening agents are generally used in dentifrice at levels of from about 0.005% to about 5%, by weight of the composition.

Non-Ionic Surfactants

Dentifrice of the present invention may optionally comprise further non-ionic surfactants. Included amongst such non-ionic surfactants are substituted polyethylene glycol ethers selected from PEG-32 Glyceryl Stearate, PEG-40 Castor Oil, PEG-60 Castor Oil and PEG-40 Sorbitan Di-Isostearate. Non-ionic surfactants generally comprise from about 0.1% to 10.0%, preferably from about 0.1% to about 4.0%, more preferably from about 0.2% to about 3.0% by weight of the composition.

Antimicrobial Agents

The dentifrice of the present invention may also include other agents, such as antimicrobial agents. Included among such agents are water insoluble non-cationic antimicrobial agents such as halogenated diphenyl ethers, phenolic compounds including phenol and its homologues, mono and poly-alkyl and aromatic halophenols, resorcinol and its derivatives, bisphenolic compounds and halogenated salicylanilides, benzoic esters, and halogenated carbanilides. The water soluble antimicrobials include quaternary ammonium salts and bis-biquanide salts, among others. Triclosan monophosphate is an additional water soluble antimicrobial agent. The quaternary ammonium agents include those in which one or two of the substitutes on the quaternary nitrogen has a carbon chain length (typically alkyl group) from about 8 to about 20, typically from about 10 to about 18 carbon atoms while the remaining substitutes (typically alkyl or benzyl group) have a lower number of carbon atoms, such as from about 1 to about 7 carbon atoms, typically methyl or ethyl groups. Dodecyl trimethyl ammonium bromide, tetradecylpyridinium chloride, domiphen bromide, N-tetradecyl-4-ethyl pyridinium chloride, dodecyl dimethyl (2-phenoxyethyl) ammonium bromide, benzyl dimethylstearyl ammonium chloride, cetyl pyridinium chloride, quaternized 5-amino-1,3-bis(2-ethyl-hexyl)-5-methyl hexa hydropyrimidine, benzalkonium chloride, benzethonium chloride and methyl benzethonium chloride are examplary of typical quaternary ammonium antibacterial agents. Preferably, when an anionic surfactant is used in the dentifrice of the present

invention, a quaternary ammonium agent is not employed. Other compounds are bis[4-(R-amino)-1-pyridinium] alkanes as disclosed in U.S. Patent 4,206,215, issued June 3, 1980, to Bailey, incorporated herein by reference. Stannous salts such as stannous pyrophosphate and stannous gluconate and other antimicrobials such as copper bisglycinate, copper glysinate, zinc citrate, and zinc lactate may also be included. Also useful are enzymes, including endoglycosidase, papain, dextranase, mutanase, and mixtures thereof. Such agents are disclosed in U.S. Patent 2,946,725, Jul. 26, 1960, to Norris et al. and in U.S. Patent 4,051,234, September. 27, 1977 to Gieske et al., incorporated herein by reference. Specific antimicrobial agents include chlorhexidine, triclosan, triclosan monophosphate, and flavour oils such as thymol. Triclosan and other agents of this type are disclosed in Parran, Jr. et al., U.S. Patent 5,015,466, issued May 14, 1991, and U.S. Patent 4,894,220, Jan. 16, 1990 to Nabi et al., incorporated herein by reference. The water insoluble antimicrobial agents, water soluble agents, and enzymes may be present. The quaternary ammonium agents, stannous salts, and substituted guanidines may be present at levels of from about 0.01% to about 1.5%, by weight of the dentifrice composition. Included among such agents are water insoluble non-cationic agents such as triclosan and other agents of the type disclosed in Parran, Jr. et al., U.S. Patent 5,015,466, issued May 14, 1991.

Abrasive

A dentifrice of the present invention optionally but preferably comprises an abrasive polishing material. The abrasive polishing material suitable for use in the compositions of the present invention can be any material which does not excessively abrade dentin. These include, for example, silicas including gels and precipitates, calcium carbonate, dicalcium orthophosphate dihydrate, calcium pyrophosphate, tricalcium phosphate, calcium polymetaphosphate, insoluble sodium polymetaphosphate, hydrated alumina, and resinous abrasive materials such as particulate condensation products of urea and formaldehyde, and others such as disclosed by Cooley et al in U.S. Pat. No. 3,070,510, issued Dec. 25, 1962. Mixtures of abrasives may also be used. Preferably the abrasive is selected from precipitated silica or silica gels.

Silica dental abrasives of various types are preferred because of their unique benefits of exceptional dental cleaning and polishing performance without unduly abrading tooth enamel or dentine. The silica abrasive polishing materials herein, as well as other abrasives, generally have an average particle size ranging between about 0.1 to about 30 microns, and preferably from about 5 to about 15 microns. The abrasive can be precipitated silica or silica gels such as the silica xerogels described in Pader et al., U.S.

Patent 3,538,230, issued Mar. 2, 1970, and DiGiulio, U.S. Patent 3,862,307, issued Jan. 21, 1975. Preferred are the silica xerogels marketed under the trade name "Syloid" by the W.R. Grace & Company, Davison Chemical Division. Also preferred are the precipitated silica materials such as those marketed by the J. M. Huber Corporation under the trade name, "Zeodent", particularly the silica carrying the designation "Zeodent 119". The types of silica dental abrasives useful in the toothpastes of the present invention are described in more detail in Wason, U.S. Patent 4,340,583, issued July 29, 1982. Suitable abrasives also include the silica abrasives described in U.S 5,651,958 and US 5,589,160. The abrasive in the dentifrice compositions described herein is generally present at a level of from about 0.1% to about 50% or above, by weight of the composition. Preferably, dentifrice contain from about 10% of abrasive, by weight of the composition.

A useful abrasive for the dentifrice of the present invention is selected such that the dentifrice has a preferred Radioactive Dentin Abrasion ("RDA") from 50 to 200. The RDA values are determined according to the method set forth by Hefferen, "Journal of Dental Research", July-August 1976, pp. 563-573, and described in the Wason US Patent Nos. 4,340,583, 4,420,312 and 4,421,527, which publication and patents are incorporated herein by reference.

Binder

The present invention compositions in the form of a dentifrice, typically contain some thickening material or binders to provide a desirable consistency. Thickening agents useful in the present invention are carboxyvinyl polymers, preferably cross-linked polyacrylates, carrageenan, hydroxyethyl cellulose, and water soluble salts of cellulose ethers such as sodium carboxymethylcellulose and sodium carboxymethyl hydroxyethyl cellulose. Natural gums such as gum karaya, xanthan gum, gum arabic, and gum tragacanth can also be used. These thickening agents can be used in an of amount from about 0.1% to about 15%, by weight of the composition.

Preferably a dentifrice of the present invention comprises a binder selected from hectorites, bentonites and fumed silica to provide a stable, easily dispersible foam.

Suitable binders for the present invention are hectorites both synthetic and natural in origin. A suitable synthetic hectorite for the present invention is sodium lithium magnesium silicate commercially available from Laporte, Southern Clay Co. under the Laponite® tradename (e.g CP, SP, D, SP2002). Natural hectorites suitable for the present invention include magnesium aluminium silicates such as Veegum which is commercially available from R.T. Vanderbilt and the montmorillonite clays which are commercially available from the Southern Clay Co. under the Gelwhite trade name,

Bentone available from Rheox, Hectabrite available from American Colloid and Hectalite, also available from American Colloid. Bentonites are also suitable binders for the present invention. Preferred are the bentonites commercially available from Southern Clay Co. under the Bentolite trade name, Whittacker Clark and Danniels under the Bentonite trade name and American Colloid under the Palar Gel trade name. Fumed or colloidal silica are further suitable binders for the present invention. Suitable silicas for the present invention are marketed under the trade names Aerosil 200 by Degussa and Cab-O-Sil M-5 available from Cabot.

The most preferred binding agent according to the present invention is the synthetic hectorite.

When the binder of the dentifrice is a hectorite, bentonite or fumed silica as described herein, it is generally present at a level of from about 0.1% to about 10% by weight of the composition. Preferably, dentifrice contain from about 0.1% to about 5.0% of binder, by weight of the composition. More preferably, dentifrice contain from 0.2% to 2.0% of binder, by weight of composition.

Preferred are dentifrice containing from about 0.1% to about 5.0% of synthetic hectorite, more preferably, the dentifrice contains from 0.2% to 2.0% of synthetic hectorite.

Peroxide Source

The dentifrice of the present invention may include a peroxide source. The peroxide source is selected from the group consisting of hydrogen peroxide, calcium peroxide, urea peroxide, and mixtures thereof. The preferred peroxide source is hydrogen peroxide. The following amounts represent the amount of peroxide raw material, although the peroxide source may contain ingredients other than the peroxide raw material. The present composition may contain from about 0.01% to about 10%, preferably from about 0.1% to about 5%, more preferably from about 0.2% to about 3%, and most preferably from about 0.3% to about 0.8% of a peroxide source, by weight of the composition.

Alkali Metal Bicarbonate Salt

The dentifrice of the present invention may also include an alkali metal bicarbonate salt. Alkali metal bicarbonate salts are soluble in water and unless stabilised, tend to release carbon dioxide in an aqueous system. Sodium bicarbonate, also known as baking soda, is the preferred alkali metal bicarbonate salt. The present composition may contain

up to 10%, preferably from about 0.5% to about 5%, more preferably from about 0.1% to about 1%.

Further Additional Components

The pH of the present dentifrice is preferably adjusted through the use of buffering agents. Buffering agents, as used herein, refer to agents that can be used to adjust the pH of the compositions to a preferred range of about pH 5.5 to about pH 10.5, more preferably about pH 3.0 to about pH 10.0. These agents include monosodium phosphate, trisodium phosphate, sodium hydroxide, sodium carbonate, citric acid, and sodium citrate. Buffering agents can be used at a level of from about 0.01% to about 10%, by weight of the present compositions.

Titanium dioxide may also be added to the dentifrice of the present invention. Titanium dioxide is a white powder which adds opacity to the compositions. Titanium dioxide generally comprises from about 0.10% to about 5%, by weight of the compositions.

The dentifrice of the present invention may also additionally comprise a short chain, saturated, hydrocarbon alcohol, wherein the short chain alcohol is selected from ethanol, propanol or butanol. Preferred is ethanol. The short chain alcohol is generally present at levels of less than about 10%, preferably less than about 5% and more preferably less than about 1%.

If desired, air may be incorporated into the dentifrice of the present invention such that the density of the unaerated dentifrice is reduced by up to 25%.

Examples

The following examples further describe and demonstrate embodiments within the scope of the present invention. For all examples, the ingredients are mixed under partial vacuum.

EXAMPLES I and II

Ingredient (% Wt/Wt)	Example 1	Example II
Water (DRO)	20.0	20.0
Sorbitol (70%), low reducing sugars	49.21	49.21
Hydrated silica, amorphous (Z119)	20.0	20.0
Carbomer 956	0.40	0.40
Xanthan gum	0.35	0.35
Laponite D	0.60	0.60
Poloxamer 188	2.0	
Poloxamer 407		2.0
Sodium alkyl sulphate, 28%	5.0	5.0
Sodium fluoride	0.24	0.24
Titanium Dioxide	0.70	0.70
Sodium saccharin	0.30	0.30
Flavour Oil	1.20	1.20
TOTAL	100.00	100.00
TOTAL WATER	38.36	38.36

Examples I and II are anticavity products and are prepared as follows. Start by combining sorbitol, xanthan gum, Carbomer and any other binders to the mixer and mix until homogeneous. Add water and Laponite D and mix until homogeneous. Next add sodium fluoride, sodium saccharin and Poloxamer. Mix thoroughly until all of the material is dissolved and check for any visible signs of lumps or undissolved material. If any undissolved material is present, gently heat the mixture, continue mixing until the material is dissolved or evenly distributed and cool the mixture to room temperature. Next pre-mix titanium dioxide into the silica. Incorporate the silica pre-mix into the vessel contents and mix until homogeneous. Lastly, pre-mix the flavour oil, and surfactant, sodium alkyl sulfate and add the pre-mix to the vessel contents. Continue mixing until the dentifrice is homogeneous.

EXAMPLE III

Ingredient	(% Wt/Wt)
Water (DRO)	52.5
Sorbitol (70%), low reducing sugars	8.79
Poloxamer 407	1.00
Glycerin	5.00
Hydrated silica, amorphous (Z119)	20.00
Carbomer 956	0.40
Xanthan gum	0.35
Laponite D	0.60
Sodium alkyl sulphate, 28%	5.00
Tetrasodium pyrophosphate	0.76
Tetrapotassium pyrophosphate, 60%	3.27
Sodium fluoride	0.32
Titanium Dioxide	0.70
Sodium saccharin	0.30
Flavour Oil	1.00
TOTAL	**100.00**
TOTAL WATER	60.05

Example III is an example of a tartar control product which is prepared as follows. Start by combining glycerin, xanthan gum, Carbomer and any other binders to the mixer to form a suspension. Add sorbitol to mixer and mix until homogeneous. Add water and Laponite D and mix until homogeneous. Next add sodium fluoride, sodium saccharin, the pyrophosphates and Poloxamer. Mix thoroughly until all the material is dissolved. If any undissolved material is present, gently heat the mixture, continue mixing until the material is dissolved or evenly distributed and cool the mixture to room temperature. Next pre-mix titanium dioxide into the silica. Incorporate the silica pre-mix into the vessel contents and mix until homogeneous. Lastly, pre-mix the flavour oil, and surfactant, sodium alkyl sulfate and add the pre-mix to the vessel contents. Continue mixing until homogeneous.

EXAMPLE IV

Example IV is an example of a multiphase product in which the first flavour containing composition and hydrogen peroxide containing compositions are prepared separately in

equal proportions and packaged into separate compartments of a dual compartment package to be dispensed therefrom.

Flavour containing composition

Ingredient	(% Wt/Wt)
Water (DRO)	37.5
Sorbitol (70%), low reducing sugars	23.83
Poloxamer 407	2.00
Glycerin	5.00
Hydrated silica, amorphous (Z119)	20.00
Carbomer 956	0.40
Xanthan gum	0.35
Laponite D	0.60
Sodium alkyl sulphate, 28%	7.50
Sodium fluoride	0.32
Titanium Dioxide	0.70
Sodium saccharin	0.30
Flavour Oil	1.50
TOTAL	**100.00**
TOTAL WATER	50.05

Hydrogen Peroxide Composition

Ingredient	(% Wt/Wt)
Water (DRO)	41.07
Glycerin	49.40
Hydrogen peroxide (35% active)	4.28
Sodium fluoride	0.24
Disodium pyrophosphate	1.00
Sodium phosphate	1.00
Carbomer 956	2.00
Xanthan gum	1.00
TOTAL	**100.00**
TOTAL WATER	43.86

EXAMPLES V to IX

The following examples (Examples V to VI) illustrate dentifrice compositions in accordance with the present invention. Examples VII to IX are comparative data illustrating examples which do not produce the claimed effect.

Example	V	VI	VII	VIII	IX
Ingredients (%Wt/Wt)					
Water (DRO)	20.0	20.0	20.0	50.0	23.39
Sorbitol (70%), low reducing sugars	48.93	48.93	46.92	16.75	43.36
Poloxamer 407	2.00	-	2.00	2.00	2.00
Poloxamer 235	-	2.00	-	-	-
Sodium alkyl sulphate, 28%	5.00	5.00	5.00	5.00	5.00
Sodium fluoride	0.24	0.24	0.24	0.24	0.24
Sodium phosphate anhydrous	-	-	0.36	-	-
Trisodium phosphate. 10H20	-	-	1.65	-	-
Tetrasodium pyrophosphate	-	-	-	1.61	1.61
Disodium pyrophosphate	-	-	-	0.56	0.56
Triclosan	0.28	0.28	0.28	0.28	0.28
Sodium saccharin	0.30	0.30	0.30	0.30	0.30
Flavour Oil	1.20	1.20	1.20	1.20	1.20
Total Liquid Carrier	77.95	77.95	77.95	77.95	77.95
Hydrated silica, amorphous (Z119)	20.0	20.0	20.0	20.0	20.0
Carbomer 956	0.40	0.40	0.40	0.40	0.40
Xanthan gum	0.35	0.35	0.35	0.35	0.35
Laponite D	0.60	0.60	0.60	0.60	0.60
Titanium Dioxide	0.70	0.70	0.70	0.70	0.70
	22.05	22.05	22.05	22.05	22.05
Visual Appearance of Liquid Carrier	Single layer	Single layer	2+ layers, top phase dark	2 layers	2 layers

Claims:

1. A dentifrice with improved flavour display comprising

   (a) from 0.1% to 10% of a flavour oil;

   (b) from 0.1% to 10% of a non-ionic block co-polymer;

   (c) from 0.1% to 5.0% of a surfactant selected from amphoteric or anionic surfactants and combinations thereof;

   (d) a fluoride ion source;

   (e) from 10% to 90% of water;

   wherein the dentifrice comprises a liquid carrier which forms a single, clear liquid layer.

2. A dentifrice according to Claim 1, wherein the non-ionic block co-polymer is selected from amine block co-polymers and polyoxyalkylene block co-polymers.

3. A dentifrice according to Claim 2, wherein the non-ionic block co-polymer is a polyoxyethylene polyoxypropylene block co-polymer.

4. A dentifrice according to Claims 1 to 3, wherein the anionic surfactant is selected from sodium lauryl sulfate, sodium lauryl sulfosuccinate, sodium lauroyl sarcosinate and sodium decyl sulfate.

5. A dentifrice according to Claim 4, wherein the anionic surfactant is sodium lauryl sulfate.

6. A dentifrice according to Claims 1 to 5, wherein the fluoride ion source is sodium fluoride.

7. A dentifrice according to any of the preceding Claims, wherein the dentifrice further comprises a binder selected from hectorites, bentonites and fumed silica.

8. A dentifrice according to any of the preceding Claims, wherein the dentifrice further comprises from 0.1% to 50% or above of an orally acceptable abrasive.

9. A dentifrice according to Claim 8, wherein an abrasive is selected from precipitated silica or silica gels.

INTERNATIONAL SEARCH REPORT

Inte tional Application No
PCT/US 99/13012

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 449 457 A (BAUSCH & LOMB) 2 October 1991 (1991-10-02) example 1	1-8
X	US 5 424 060 A (HAUSCHILD JOHN P) 13 June 1995 (1995-06-13) claims; example 3	1-8
X	WO 97 11675 A (COLGATE PALMOLIVE CO) 3 April 1997 (1997-04-03) examples	1-6,8
P,X	EP 0 868 903 A (BASF CORP) 7 October 1998 (1998-10-07) claims	1-6,8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 October 1999	14/10/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Couckuyt, P

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INTERNATIONAL SEARCH REPORT

Inte tional Application No
PCI/US 99/13012

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 476 107 A (SCHMOLKA IRVING R) 9 October 1984 (1984-10-09) the whole document	1-6,8

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter tional Application No
PCI/US 99/13012

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0449457 A	02-10-1991	US 5028413 A	02-07-1991
		AT 105178 T	15-05-1994
		CA 2038625 A	22-09-1991
		DE 69101868 D	09-06-1994
		DE 69101868 T	18-08-1994
		JP 4217619 A	07-08-1992
US 5424060 A	13-06-1995	US 5374368 A	20-12-1994
		CA 2150426 A,C	07-12-1995
		US 5496542 A	05-03-1996
		US 5676933 A	14-10-1997
WO 9711675 A	03-04-1997	AU 701758 B	04-02-1999
		AU 7243896 A	17-04-1997
		CA 2233006 A	03-04-1997
		CN 1200665 A	02-12-1998
		US 5851514 A	22-12-1998
EP 0868903 A	07-10-1998	US 5855874 A	05-01-1999
		US 5908612 A	01-06-1999
		AU 4853497 A	02-07-1998
		CA 2216978 A	30-06-1998
		JP 10316549 A	02-12-1998
		CA 2216749 A	30-06-1998
US 4476107 A	09-10-1984	CA 1225932 A	25-08-1987